

“On the Elimination of Alcohol.” By A. DUPRÉ, Ph.D., Lecturer on Chemistry at Westminster Hospital. Communicated by WILLIAM ODLING, M.B., F.R.S. Received November 16, 1871*.

Previous to the year 1860 it was the generally received opinion that the greater portion of any alcohol taken was oxidized in the system, and only a small fraction eliminated unaltered. In that year, however, Messrs. Perrin and Lallemand published an elaborate memoir on the subject, in which they maintained that all, or at least nearly all, the alcohol taken is eliminated unaltered. This opinion was soon very generally adopted, notwithstanding the fact that Messrs. Perrin and Lallemand never succeeded in recovering, from the excretions, more than a very small fraction of the alcohol consumed, although very large doses were frequently given. However, the missing alcohol was easily accounted for as loss, occasioned by its ready volatility.

Soon after Dr. Anstie took up the subject, and, on the strength of numerous qualitative experiments, arrived at the conclusion, which he was the first to publish in this country, that the originally received opinion was correct, viz. that a small portion only of any alcohol taken is eliminated unaltered. After this, Dr. Thudichum and the author in this country, and Ichulinus abroad, undertook a number of quantitative experiments which proved that a minute fraction only of the alcohol taken is eliminated through the kidneys. Owing to these researches, general opinion gradually reverted to the original notion.

Quite recently, however, Drs. Parkes and Wollowicz have published several valuable memoirs on the action of brandy, alcohol, and wine on the human body, in which they adopt, at least partially, the views of Messrs. Perrin and Lallemand. But here also no quantitative results are given which will account, even approximately, for the amount of alcohol supposed to be eliminated. Drs. Parkes and Wollowicz believe that the elimination of alcohol may go on for 5 or 6 days after the last dose of alcohol has been taken; and they express the opinion that Dr. Anstie and the author, by assuming that elimination practically ceases after 24 hours, had considerably underestimated the amount actually eliminated. The author has thereby been induced once more to investigate this subject.

Assuming, then, for the sake of argument, that all the alcohol is eliminated, and that such elimination takes 10 days†, it would follow that if a certain quantity of alcohol be taken daily, the amount eliminated would increase from day to day until, from the 10th day onward, the quantity

* Read January 25, 1872. (For abstract see p. 107.)

† This seems the very utmost limit that can be conceded. In the numerous experiments of Dr. Bence Jones and the author, on the passage of substances into and out of the tissues, it was found that the elimination of lithium, for example, was complete in 5 to 6 days, while all elimination of quinine ceased after 2 days. In neither case did any of the substance remain behind.

eliminated daily would equal the daily consumption ; in other words, the quantities which would be eliminated, if this theory were correct, might be measured by ounces instead of by grains, and even the most ordinary processes of analysis could not fail to yield considerable quantities of alcohol. The argument loses nothing in force if it be contended that elimination lasts longer than 10 days ; for, however long it may last, if the alcohol diet is continued, a time must come when elimination and consumption would be equal. Obviously, however, there is a tolerably narrow limit given to the time during which elimination can be presumed to last ; for the alcohol, if not eliminated, must accumulate in the body, and would speedily rise to a proportion totally incompatible with life itself. The experiments recorded in the following pages were guided by the foregoing considerations.

Analytical processes employed.—Since, in the experiments of Messrs. Perrin and Lallemand, the alcohol not recovered is accounted for as loss, the author has thought it of importance to give the analytical processes employed in greater detail than might otherwise be considered necessary. It will thus be shown how much of the alcohol present can be recovered, and how much may reasonably be accounted for as loss. Alcohol is eliminated through four channels,—kidneys, lungs, skin, and bowel.

Examination of the Urine.—The urine to be examined is rendered slightly acid by dilute sulphuric acid ; some tannin is added to prevent frothing, and about $\frac{1}{3}$ of it is distilled over. This first distillate is now made slightly alkaline by caustic potash or soda, and redistilled ; this second distillate is once more acidified by sulphuric acid, and again distilled, $\frac{1}{3}$ being driven over each time. If these three distillations reduce the amount of liquid to about 20 cub. centims., it may at once be submitted to oxidation. If, however, the amount of urine employed was so large that this third distillate amounts to much more than 20 cub. centims., the redistillation must be repeated until the quantity is brought down to 20 cub. centims. Less than three distillations should, however, in no case be made. All distillations should, moreover, be conducted with an apparatus in which both retort and receiver are connected air-tight with the condenser, the receiver being furnished with a safety-tube closed by a globule of mercury. The final distillate is now put into a small assay flask, a suitable amount of bichromate solution is added, the flask is closed by a well-fitting caoutchouc-stopper tied down, and heated for one hour in a water-bath. The flask is then taken out, cooled, opened, and the excess of bichromate left is reduced by zinc. (The bichromate solution is made by dissolving 147 grammes of potassium bichromate in water, adding 200 grammes of strong sulphuric acid, and making up the solution to 1400 cub. centims. Ten cub. centims. of this solution will oxidize nearly 0.2 gramme alcohol into acetic acid. After a little practice, it is easy to judge by the colour of the liquid in the flask whether or no sufficient bichromate had been added.) When all the bichromate is reduced, the green solution

is transferred to a small retort, some sulphuric acid is added, and the acetic acid present is distilled over. To do so effectually, the distillation is continued almost to dryness, some water is then added to the residue, and the distillation resumed; this is repeated three times. The distillation may be conducted over an Argand burner, and sometimes it is advisable to place pieces of tobacco-pipe into the retort to avoid bumping. In the distillate the acetic acid is now estimated by a standard solution of deci-normal soda, 1 cub. centim. of which neutralizes 0.006 grm. acetic acid, and indicates therefore 0.0046 grm. of alcohol. If ordinary care has been used, no trace of sulphuric acid will be present in the distillate; but if the distillation has been carried too far, so that the residue in the retort has become dry, traces of sulphuric acid may have passed into the distillate. In such case the acidity of the distillate is carefully estimated, and the neutral solution is evaporated to dryness on a water-bath. To the dry residue an amount of deci-normal sulphuric acid is added slightly in excess of the quantity of deci-normal soda used, and the resulting solution is once more evaporated on the water-bath. During this second evaporation all the acetic acid is driven off. The acidity of the residue is now determined as before, and will be found equal only to the excess of deci-normal acid taken, in case nothing but acetic acid (or other volatile acid) was present in the distillate. If, however, any sulphuric acid had passed over, the acidity of this residue will be found greater than the excess of deci-normal acid added, and this surplus is the measure of the sulphuric acid contained in the distillate. If this then is subtracted from the total acidity originally found, the rest will be the acetic acid. If an appreciable amount of volatile acid is present, which to a great extent may be judged of by the colour of the bichromate solution after the heating, the disturbing effect of any sulphuric acid having passed over may also be neutralized in the following manner. The distillate is accurately divided into two equal parts; the acidity of the one half is estimated directly, the other half is evaporated on a water-bath, and the acidity of the residue left is determined. The difference between these two determinations will give the volatile acid present in one half of the distillate. Lastly, the acetic acid may be estimated by neutralizing the distillate by pure barium carbonate, filtering, washing, &c., evaporating the solution to dryness, and weighing the barium acetate left. The above process yields accurate results, even with very small quantities of alcohol; thus in two check experiments the amount of alcohol taken was 0.1 and 0.025 gramme, the acetic acid obtained neutralized 20.1 cub. centims. and 5.5 cub. centims. of deci-normal soda, corresponding respectively to 0.0924 and 0.0253 gramme of alcohol.

Examination of Breath.—By help of a suitable mouthpiece the breath is blown, through a wide tube containing chloride of calcium, into a bag placed between light-pressure boards (such a bag as is used in the administration of laughing-gas, and holding from 4 to 5 cubic feet). From this bag it passes into a flask containing water, thence into a Liebig's con-

denser in connexion with a receiver, and finally escapes into the air. The experiment is conducted as follows :—The bag being empty, the water in the flask is heated to boiling, and the breath is blown into the apparatus for a quarter to half an hour. The breath is first deprived of most of its moisture by the chloride of calcium, and next enters the bag dry, or nearly so. From the bag it passes, at considerably reduced speed, through the flask, where it becomes mixed with steam, into the condenser. In this last the steam is condensed, and with it the greater part of the alcohol vapours present. The alcohol will therefore be found in the distilled water collected in the receiver. When the breath has been blown into the apparatus during the desired length of time, the blowing is discontinued, the tube is closed by a clamp, and the air collected in the bag is allowed to pass gradually through the retort and condenser. The chloride of calcium is now dissolved in water, the solution is added to the distillate collected, and the alcohol therein contained is estimated by repeated distillations, oxidation, &c., as described in the case of urine. If it is desired to blow for a greater length of time than half an hour, it is necessary, with a bag of the above size, to blow it up twice, each time of course allowing all the air collected to pass out through the retort and condenser. At first it is difficult to keep up the ordinary rate of respiration while blowing into the bag; but with a little practice this becomes easy, and a bag holding about 4 cubic feet will then suffice for half an hour's breathing. At the end of this time about 4 cubic feet of air should be in the bag, while 2 cubic feet have passed through the apparatus; the bag will then take one hour more to become empty. The bag has thus to serve both as a reservoir and regulator, reducing the velocity of the air-current to about one third. The desired velocity is readily obtained by a proper adjustment of the weights on the pressure-boards. The boiling of the water in the flask is regulated so as to give about half a litre distilled water for every 12 cubic feet of air passing through. The breath was blown through the apparatus for half an hour. The following quantitative experiments, made under precisely the same conditions as the experiments with the breath, will serve to show that the greater part of the alcohol carried by the air is condensed with the steam. A given quantity of alcohol was evaporated in a current of air, which was afterwards passed through the apparatus at the same speed as the breath. In the distillate obtained, the alcohol was estimated as described. The amount of air taken was 12 cubic feet, equivalent to about one hour's breathing, and necessitated the filling of the bag twice.

First experiment.—Amount of alcohol evaporated 0·004 gramme; acetic acid obtained neutralized 0·67 cub. centim. d. n. soda, equivalent to 0·031 gramme alcohol.

Second experiment.—Amount of alcohol evaporated 0·008 grm.; acetic acid obtained neutralized 1·25 cub. centim. d. n. soda, equivalent to 0·0058 grm. alcohol.

Third experiment.—Amount of alcohol evaporated 0·0415 grm.; acetic

acid obtained neutralized 6.05 cub. centim. d. n. soda, equivalent to 0.0278 grm. alcohol.

In the first two experiments $\frac{3}{4}$, in the last $\frac{2}{3}$ of the alcohol contained in the 12 cubic feet of air was recovered in the distillate. In a blank experiment, in which air only was blown through the apparatus, no trace of volatile acid was obtained.

Examination of Alvine Discharges.—These are stirred up with water, the mixture is distilled &c., and the alcohol in the final distillate is estimated as described. In the experiments recorded in the following Tables, the alvine discharges were not examined, previous experiments having convinced the author that, even in cases where very large quantities of brandy are taken for some length of time, the amount of alcohol eliminated by the bowel is extremely small.

Examination of Cutaneous Exudations.—No attempt was made to estimate the amount of alcohol eliminated by the skin. Qualitatively, however, the fact that traces of alcohol are thus eliminated may be shown as follows:—Part of the body is enclosed for several hours in an air-tight covering; at the end of that time the perspiration collected is washed off with clean water, the distillate from which is then tested with bichromate and strong sulphuric acid. Dr. Anstie has made numerous experiments in this manner, which show conclusively that the amount so eliminated is always extremely minute. The actual amount eliminated might perhaps be estimated, with tolerable exactness, by enclosing an ascertained fraction of the entire surface of the body in an air-tight bag, through which a current of dry air is passed. In this air the alcohol is then determined exactly as in the case of the breath.

By means of the method just described, two series of experiments on the elimination of alcohol were made, and, for the sake of absolute certainty, the author conducted them in his own person.

First Series.—Having first abstained absolutely, for a space of 10 days, from all alcoholic drinks or other articles of food containing alcohol, the urine was collected on the 11th day, and the breath blown through the apparatus for half an hour. On the 12th day, and on each of the twelve succeeding days, 112 cub. centims. of brandy* were taken daily (28 cub. centims. at 1 P.M., 56 cub. centims. at 6 P.M., and 28 cub. centims. at 11 P.M.). The urine was collected between the hours of 3 P.M. one day and 3 P.M. the following day, on 1st, 6th, and 12th day of the brandy diet, and 4 P.M. on the same above-mentioned days. Lastly, the urine was collected during the 5 days following the cessation of the brandy diet. The analytical results obtained are arranged in the following Table.

* The brandy contained 43.47 per cent. by weight of absolute alcohol.

TABLE I.—Left off taking alcohol February 26, 1871; first cub. centim. of brandy taken March 8th at 6 P.M.

Date.	Cubic centimetre deci-normal soda neutralized by acetic acid obtained from		Amount of alcohol, corresponding to this acid, discharged in 24 hours, in grammes, through		Amount of absolute alcohol taken in the 24 hours.
	$\frac{1}{2}$ hour's breath.	24 hours' urine.	Breath.	Urine.	
March 8	0.03	0.67	0.0083	0.0031	None.
„ 9	0.05	9.44	0.0138	0.0434	52.16
„ 14	0.05	7.80	0.0138	0.0359	52.16
„ 20	0.04	5.00	0.0110	0.0230	52.16
„ 21	0.64	0.0029	None.
„ 22	0.29	0.0013	„
„ 23	0.40	0.0018	„
„ 24	0.50	0.0023	„
„ 25	0.45	0.0021	„

Total amount of absolute alcohol taken during the twelve days 625.92 grms.

Total amount of absolute alcohol discharged by the kidneys during the same twelve days, 0.3984 grm., taking the daily elimination at 0.0332 grm., the mean of that on the 1st and 12th day.

Total amount of absolute alcohol eliminated by the lungs, taking the amount discharged at 3 P.M. on the 14th as representing the mean elimination during the day, and adding $\frac{1}{3}$ for loss, as shown by the control experiments, 0.2064 grm.

TABLE II.—56 cub. centims. brandy (26.08 grms. absolute alcohol) taken 10 A.M. March 29th.

Period of elimination.	Alcohol eliminated by breath during 1 hour		Alcohol eliminated by breath during entire period.	Quantity of urine discharged in cub. centims.	Alcohol eliminated in the urine.	
	Yielded \bar{A} , which neutralized cub. centim. deci-normal soda.	Equivalent to grammes of alcohol.			\bar{A} obtained neutralized cub. centim. deci-normal soda.	Equivalent to grammes of alcohol.
First 3 hours.....	6.9	0.03174	0.09522	570	36.36	0.16720
Second 3 hours	0.3	.00138	.00414	92	.63	.00290
Third 3 hours	0.25	.00115	.00345	180	.45	.00207
Fourth 3 hours	120	.05	.00023
Next 12 hours	350	.36	.00166
1st day following...	0.25	.00115	.02760	900	.40	.00184
2nd day following...	0.25	.00115	.02760	1050	.46	.00212

Second series.—Discontinued the use of alcohol, in any shape, on March the 20th. On March the 29th, at 10 A.M., took 56 cub. centims. brandy (same brandy as in previous experiments). Urine collected for every 3 hours up to the 12th, from the 12th to the 24th hour, and during the next succeeding 2 days. The breath was passed through the apparatus, for ten minutes at a time, in every half hour during the first 9 hours, and during 1 hour (between 2 and 4 P.M.) on the 2 days following. The results are arranged in Table II. p. 273.

Total amount of absolute alcohol eliminated through the kidney during the 3 days 0·1780 grm.; more than $\frac{9}{10}$ of this amount was eliminated during the first 3 hours.

Total amount of absolute alcohol eliminated through the lungs during the 3 days (adding $\frac{1}{3}$ for loss) 0·2336 grm. In both cases all the volatile acid obtained during the 3 days is calculated as alcohol.

An examination of Table I. shows that, even after 10 days' total abstinence, a substance is eliminated by the kidneys, and apparently also in the breath, which, when distilled and oxidized, yields a volatile acid (the acid has the smell of acetic acid). An opportunity was therefore taken to examine the urine of a gentleman, a teetotaler, who had only once in his life, and that two years previously, taken some spirituous liquor. On treating this urine in the usual manner, for the detection and estimation of alcohols, an amount of volatile acid was obtained from 1 day's urine which neutralized 0·5 cub. centim. deci-normal soda. The experiment was twice repeated with different days' urine with the same result. The smell of the volatile acid in this case also was that of acetic acid. We must therefore look upon this substance, whatever it may be, which yields the volatile acid as a normal constituent of urine. The elimination of alcohol must, then, be considered at an end as soon as the proportion of volatile acid obtained sinks to the normal amount.

Leaving, then, the nature of this substance out of consideration for the present, we arrive at the following conclusions:—

1st. The amount of alcohol eliminated per day does not increase with the continuance of the alcohol diet; therefore all the alcohol consumed daily must of necessity be disposed of daily; and as it certainly is not eliminated within that time, it must be destroyed in the system.

2nd. The elimination of alcohol following a dose or doses of alcohol is completed 24 hours after the last dose has been taken.

3rd. The amount of alcohol eliminated, in both breath and urine, is a minute fraction only of the amount of alcohol taken*.

A consideration of Table II. leads substantially to the same conclusions. Here, a single dose having been taken, elimination had ceased to be per-

* Quite recently I have examined the urine of a woman suffering from ascites, who at the time of the experiment took 12 ounces of brandy (38 per cent. by weight of absolute alcohol) daily, and had done so during a period of six weeks. Two days' urine yielded 0·0366 grm. of acetic acid, equivalent to 0·02806 grm., or 0·44 grain alcohol.

ceptible; that is, the amount of volatile acid yielded on oxidation had sunk to the normal amount 9 hours after the dose had been taken. The proportion of alcohol eliminated in this second experiment, although still small, is, however, considerably higher than it was in the first; but this is most likely owing to the different conditions under which the experiment was made. The two ounces of brandy were taken within a very short space of time and early in the morning, no other food being taken at the same time. In consequence of this, the brandy had a considerable diuretic effect during the first few hours, within which, as will be seen, more than $\frac{9}{10}$ of the total proportion was eliminated.

It has been shown in the foregoing that urine, even after 10 days of total abstinence, when treated as for the estimation of alcohol, yields some volatile acid which, as judged by the smell, is acetic acid. A similar substance was also found in the urine of a teetotaler; and a preliminary experiment having shown that at least the greater part of this substance passed over with the first portions of distillate, a somewhat larger quantity of the same urine was obtained and examined. The total quantity employed amounted to 180 ounces, being the greater part of 10 days' urine. To avoid decomposition, the daily portion of urine was at once acidified slightly, and $\frac{1}{3}$ of it distilled; this distillate was rendered alkaline and re-distilled. At the end of the 8 days, all these distillates were mixed, acidified, and again distilled. This third portion was now twice distilled over freshly ignited animal charcoal, after which the distillations were repeated until the quantity of liquid was reduced to 10 cub. centims., care being taken that never less than $\frac{1}{3}$ was driven over. All the distillations were, moreover, conducted with the usual precautions of having the receiver closed by a mercury valve. These 10 cub. centims. showed the following properties:—

Specific gravity at 15°·5 C., 0·9996 water at the same temperature taken as unity. Vapour-tension in Geissler's vaporimeter equivalent to 0·88 per cent. by weight of alcohol.

3·593 of it, when oxidized by bichromate &c., yielded an acid distillate which, when neutralized by barium carbonate, filtered and evaporated, gave 0·0192 gm. barium salt; this barium salt, on decomposition with sulphuric acid, gave 0·0176 gm. of barium sulphate, and contained therefore 53·88 per cent. of barium; pure barium acetate contains 53·72 per cent. barium. The acid vapours expelled had the smell of acetic acid. Another portion readily gave the emerald-green reaction with bichromate and strong sulphuric acid, and finally they readily gave the iodoform test, viz. when treated with iodine and an alkali, a yellow glittering precipitate was produced, which, under the microscope, consisted of golden-coloured six-sided plates, sometimes single, sometimes united into stars in the manner of snow-crystals.

The author having again abstained from the use of alcohol since May the 16th, the urine was collected from May the 29th to June the 10th

(with the exception of June the 4th and 5th), amounting altogether during the 10 days to 360 oz. This urine was treated exactly as the previous sample, and the amount of distillate finally collected was also 10 cub. centims; these 10 cub. centims. possessed a specific gravity of 0.9988 at 15°5 C.

In Geissler's vaporimeter they showed a vapour-tension equivalent to 1.7 per cent. by weight of alcohol; 3.588 grms. of it, when oxidized &c., gave 0.0307 grm. barium salt, yielding 0.0278 grm. barium sulphate, and contained therefore 53.24 per cent. of barium: here also the smell of the escaping acetic acid was unmistakable. The volatile acid obtained from another portion of these 10 cub. centims. gave with ferric chloride distinctly, though but feebly, the well-known reaction of acetic acid. Finally, they gave readily the iodoform test, as well as the green reaction, with bichromate and strong sulphuric acid.

On June the 22nd and 23rd the urine was again collected and examined, no alcohol having been taken since May the 16th. The urine of the 22nd yielded an amount of acid neutralizing 0.53 cub. centim. deci-normal soda, the volatile acid produced from the distillate of the urine on the 23rd neutralizing 0.55 cub. centim. of the same soda. Lastly, the urine was collected on June the 26th, 27th, and 28th, no alcohol whatever having been taken since May the 16th. The urine was repeatedly distilled, as usual, the final distillate amounting to 5 cub. centims.; these 5 cub. centims. readily gave the iodoform test, as well as the green reaction, with bichromate and strong sulphuric acid.

It appears, therefore, that a substance is found in the urine after six weeks' total abstinence, and even after an abstinence of two years, which gives the reactions ordinarily employed for the detection of small quantities of alcohol. Since it is impossible to assume that any elimination of alcohol, due to alcohol which has been taken, could go on for a period of six weeks, not to speak of two years, we must conclude that this substance is a normal constituent of human urine, or at least may be obtained from it by distillation with dilute acid &c. At first the author inclined to the belief that this substance is actually ethylic alcohol, although the very small quantities dealt with did not allow of its separation. The final distillate obtained is, however, evidently a mixture; and it would therefore be unsafe to rely solely on the above test as a sufficient demonstration of the presence of alcohol, more particularly as the proportion of alcohol, as calculated from the specific gravity, differs widely from that derived from the vapour-tension, and neither agree with the proportion as calculated from the amount of acetic acid obtained by oxidation. Moreover, the distillate yields the iodoform test far more readily than would correspond to its alcoholic strength as calculated by any of the above processes, and the appearance of the precipitate also differs somewhat from that produced in pure dilute alcohol. However, while still engaged in the examination of this substance, the author learned that M. Lieben, to whom we owe the introduc-

tion of the iodoform test, had already discovered the presence of a volatile substance in human urine, as well as in that of various animals, which gives the iodoform test. Working on larger quantities of urine, he has arrived at the conclusion that this substance is not alcohol. M. Lieben also has failed to isolate and identify the substance, owing to the very small quantity present in the urine; he thinks, however, that it may be one of the odoriferous constituents of the urine. According to the author's experience this cannot, however, be the case, since, first, the quantity of substance yielding the iodoform does not seem to be diminished by distillation over animal charcoal, whereas the urinous odour is thus almost entirely removed; secondly, the urinous odour of the distillate, in case no animal charcoal was used, is not destroyed by heating with the bichromate solution, which nevertheless produces acetic acid; thirdly, a somewhat similar substance seems present in the breath. It might be, however, that the substance giving the iodoform test and that yielding the acetic acid are two different compounds; this must be left to future researches to decide.

In conclusion, it may not be uninteresting to point out that the quantity of substance which yields the acetic acid apparently falls below the normal proportion just after the effect of a dose or doses of alcohol has passed off; after which it gradually rises again to the normal standard. A somewhat analogous effect was observed by Dr. Bence Jones and the author, in their research on the passage of quinine into and out of the tissues &c., to follow the administration of quinine. In this case the natural fluorescence of the extracts from the tissues, due to the presence of a substance resembling quinine, and therefore called animal quinoidine by the discoverers, frequently fell below the normal standard just after the effect of the quinine had passed off, gradually rising again to the normal proportion. A closer study of this relation might perhaps throw considerable light on the physiological action of alcohol both in health and in disease.

April 11, 1872.

The EARL OF ROSSE, D.C.L., Vice-President, in the Chair.

The following Letter was read :—

Whitehall, 23rd February, 1872.

SIR,—I have had the honour to lay before the Queen the loyal and dutiful Address of the President, Council, and Fellows of the Royal Society on the occasion of the illness of His Royal Highness the Prince of Wales.

I have to inform you that Her Majesty was pleased to receive the Address very graciously.

I am, Sir, your obedient Servant,

(Signed) H. A. BRUCE.

*W. Sharpey, Esq., M.D., Secretary to the Royal Society,
Burlington House, W.*